REMARKS

Claims 1-6, 8, and 16-27 are examined in this case. These claims stand rejected under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 103. In addition, claims 1-6, 8, and 16-25 stand rejected under 35 U.S.C. § 102. These rejections are addressed below.

Amendments

Claim 1 has been amended to recite a particular combination of polyphenols for treatment of a patient suffering from actinic keratosis. This amendment finds support in the specification, for example, page 12, lines 9-11, page 13, lines 9-11, and page 17, lines 3 and 22. All other amendments merely conform the claim language to amended independent claim 1. These amendments add no new matter.

For the record, Applicants do not agree with the present rejections and reserve the right to pursue all cancelled subject matter in future, related applications.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-6, 8, and 16-27 stand rejected as failing to comply with the written description requirement. This rejection is based on the Office's assertion that the claimed mixture of phenols is not supported by the specification. This rejection is respectfully traversed.

As amended, claim 1 is directed to a mixture of polyphenols containing the following specific components: (-)-epicatechol, (-)-epicatechol gallate, (-)-epigallocatechol, (-)-epigallocatechol gallate, and (-)-gallocatechol gallate. Support for this mixture is found in the specification, for example, at page 12, lines 9-11, where it states:

> Preferred catechols employed in the present invention are (-)-epicatechol, (-)-epicatechol gallate, (-)-epigallocatechol, (-)-epigallocatechol gallate, (+)-gallocatechol and/or (-)-gallocatechol gallate.

Further, this combination is present in the particular mixture described on page 13, lines 9-11, as Polyphenon® E. As indicated, this mixture contains (-)-epicatechol, (-)-epicatechol gallate, (-)-epigallocatechol, (-)-epigallocatechol gallate, and (-)-gallocatechol gallate. The rejection based on lack of written description should be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-6, 8, and 16-25 also stand rejected as being anticipated by either D'Jang (U.S. Patent 5,910,308) or Hsu (US Patent Publication 2004/0191842). As applied to the amended claims, these rejections are respectfully traversed.

Independent claim 1 is now directed to a method of treating actinic keratosis that involves administering to a patient having an actinic keratosis a mixture of polyphenols containing the following specific components: (-)-epicatechol, (-)-epicatechol gallate, (-)-epigallocatechol, (-)-epigallocatechol gallate, and (-)-gallocatechol gallate.

D'Jang does not disclose treatment of actinic keratoses using a mixture of polyphenols. In fact, D'Jang does not discuss treatment of actinic keratoses by any means. D'Jang instead teaches only that green tea extracts are known to be used to treat skin cancer (see col. 2, lines 18-19). As previously indicated, actinic keratosis is a condition that can sometimes develop into squamous cell carcinoma (page 1, lines 26-27 of the specification). It is thus a precursor of cancer, but not a cancer (page 3, lines 1-2 of the specification). The Office has not disputed this point, but has stated that the "claims are not limited to a patient suffering from actinic keratosis, just a patient." Independent claim 1 has been amended to clarify that the method is directed to "treating a patient with an actinic keratosis." The § 102 rejection over D'Jang should be withdrawn.

Claims 1-6, 8, and 16-25 stand further rejected as anticipated by Hsu (U.S. Patent Publication 2004/0191842). The Office states:

> Hsu teaches a mixture of green tea polyphenols which are used topically in ointment form to treat actinic keratosis, see claims, paragraphs 65 and 66. Hsu also teaches that an additive such as a wax can also be included with the composition, see paragraph 85. The concentrations and types of green tea polyphenols are inherent to the green tea extract. No special method of extraction of the polyphenols from the green tea is disclosed in the instant specification thus the green tea disclosed in Hsu must contain the same polyphenols and in the same amounts as claimed.

This rejection is respectfully traversed. As indicated on its face, the Hsu reference is a publication of a U.S. application filed December 10, 2003, which claims the benefit of a provisional application filed December 10, 2002. Applicants' effective filing date intervenes, falling on October 9, 2003. Thus, the only subject matter in Hsu that constitutes prior art to the claimed invention under 35 U.S.C. § 102(e) is material disclosed in the Hsu provisional application. For the Examiner's convenience, a copy of that priority document is submitted herewith. A review of the Hsu utility application and its priority document indicates clearly that the support relied upon above for the § 102 rejection is absent from that priority application. Paragraphs 65, 66, and 85 were all added after Applicants' filing date, as were claims directed to actinic keratosis.

Moreover, there is no support for the statement that the Hsu green tea extract contains the same polyphenols as claimed by Applicants. Indeed, quite to the contrary, Hsu repeatedly teaches that their compositions contain four polyphenols, rather than the five components claimed by Applicants. Specifically, nowhere does Hsu indicate that their extract includes (-)-gallocatechol gallate.

In addition, the Hsu priority document focuses on screening methods for cancer therapeutics. The document is entitled "The Use of p57/KIP2 to Evaluate Agents for the Treatment and Prevention of Cancer," and the claims are similarly limited. The sole disclosure to actinic keratosis at page 84 is purely theoretical and states that green tea components "may" be useful topically for treatment of epithelial conditions such as actinic keratosis and "might" be beneficial to patients who have conditions characterized by abnormally accelerated skin cell growth and lack of differentiation. Hsu goes on to qualify these theoretical statements as follows:

> However, ***future studies are needed*** to determine the optimal time of treatment, concentrations and ***combinations of green tea polyphenols*** to be used topically for therapeutic intervention for various epithelial conditions.

Thus, as of December 10, 2002, the Hsu teaching constitutes nothing more than a theoretical statement about what might be possible with further research. This theoretical statement lacks information about the specific combination of polypenols to be used for treatment of actinic keratoses and makes a clear qualification that future studies are needed to determine what those combinations might be.

In contrast, Applicants in their specification provide, for the first time, a specific teaching of a polyphenol combination to be used for actinic keratosis treatment, complete with human experimental data demonstrating the success of their claimed polyphenol combination.

The § 102(e) rejection over Hsu should be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1-6, 8, and 16-27 stand further rejected, under 35 U.S.C. § 103(a), as being unpatentable over either D'Jang in view of Miller et al. (US Patent Publication 2004/0181130); Linden et al. (Recent Results in Cancer Res. 163:165, 2003) in view of D'Jang and Miller; or Hsu in view of Miller. These rejections are respectfully traversed.

Taking each in turn, as indicated above, D'Jang fails to disclose anything about treatments for actinic keratosis. Instead, D'Jang teaches the use of an herbal extract-based composition containing *Gynostemma pentaphyllum,* green tea, and hawthorn berry extracts for the treatment of skin cancer. As noted above, actinic keratosis is not a skin cancer. The secondary reference, Miller, does not cure this deficiency. Miller is cited as disclosing the use of curettage for the treatment of actinic keratosis. Miller does not teach that actinic keratosis is a skin cancer, nor does Miller indicate in any way that curettage should be used with Applicants' particular polyphenol combination for the treatment of actinic keratosis. The rejection based on D'Jang and Miller should be withdrawn.

Claims 1-6, 8, and 16-27 also stand rejected, under 35 U.S.C. § 103(a), as being unpatentable over Linden et al. in view of D'Jang and Miller et al. As acknowledged by the Office, Linden does not teach administration of a mixture of particular polyphenols, but instead teaches administration of the single compound epigallocatechin gallate. Moreover, this compound is only proposed as a good candidate agent for chemoprevention of human nonmelanoma skin cancer (see page 166, last sentence to page 167, first full paragraph; see also Linden et al. (2002) Tumor Prevention and Genetics, S21 as enclosed). In addition, Linden teaches that in the formulation described in the reference, this compound was minimally effective or ineffective in human tests on actinic keratosis. Specifically, Linden states (at pages 170-171);

> Our study of epigallocatechin gallate for the treatment of actinic keratoses has shown minimal to no clinical activity; however, this might be attributable to the particular formulation used.

The remaining references do not cure this deficiency. D'Jang fails to disclose anything about treatments for actinic keratosis. And Miller teaches only the use of curettage for actinic keratosis treatment. This § 103 rejection as well should be withdrawn.

Claims 1-6, 8, and 16-27 also stand rejected as being unpatentable over a combination of Hsu and Miller. As indicated above, the passages relied upon for support of this rejection were added in the Hsu utility filing of December 10, 2003 and do not constitute prior art to the present claims, which have an effective filing date of October 9, 2003. Moreover, the sole disclosure in the Hsu priority document relating to actinic keratosis is a theoretical comment regarding the possible use of green tea polyphenols. The priority document provides no information regarding particular polyphenol combinations that would be efficacious, and, in fact, Hsu states that further studies would be needed to identify those combinations. Miller, a reference teaching only the use of curettage, does not provide what Hsu lacks. Accordingly, the obviousness rejection in view of Hsu and Miller should also be withdrawn.

Notification of Potential Interfering Subject Matter

Applicants draw the Examiner's attention to the published claims of Hsu, US Patent Publication 2004/0191842 and point out that the above-referenced application may claim subject matter that is considered identical or overlapping with subject matter contained in that Hsu patent application.

Information Disclosure Statements

Applicants again note that the Forms PTO 1449 that were submitted with Information Disclosure Statements filed on November 18, 2003, February 17, 2005, and July 27, 2005 have not been initialed and returned, and hereby request that they be initialed and returned with the next Office action.

CONCLUSION

Applicants submit that this case is now in condition for allowance, and such action is respectfully requested.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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